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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/560,501

06/15/2006

Vamsi Krishna Mootha

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EXAMINER

HAMA, JOANNE

ART UNIT

PAPER NUMBER

1632

MAIL DATE

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

## Office Action Summary

**Application No.**

10/560,501

**Applicant(s)**

MOOTHA ET AL.

**Examiner**

Joanne Hama, Ph.D.

**Art Unit**

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 15 June 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-7, 11-17, 19-21, 35-38, 42-48, 78 and 93 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) \_\_\_\_\_ is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☒ Claim(s) 1-7, 11-17, 19-21, 35-38, 42-48, 78 and 93 are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_.

This Application, filed June 15, 2006, is a 371 of PCT/US04/19017, filed June 14, 2004, which claims priority to U.S. Provisional Applications 60/478,238, filed June 13, 2003, 60/525,548, filed November 26, 2003, and 60/559,141, filed April 2, 2004.

Amendments to the claims were filed December 12, 2005. Claims 4, 5, 12-15, 19, 37, 45, 47, 48, are amended. Claims 8-10, 18, 22-34, 39-41, 49-77, 79-92, 94-105 are cancelled.

Claims 1-7, 11-17, 19-21, 35-38, 42-48, 78, 93 are pending.

Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group 1, claim(s) 1-7, 11-16, drawn to a method of modulating a biological response in a cell, the method comprising contacting the cell with at least one agent that modulates the expression or activity of Err-alpha or Gabp.

Group 2, claim(s) 17, 19-21, drawn to a method of determining if an agent is a potential agent for the treatment of a disorder that is characterized by glucose intolerance, insulin resistance or reduced mitochondrial function.

Group 3, claim(s) 35-38, drawn to a method of reducing the metabolic rate of a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of an agent.

Group 4, claim(s) 42-46, drawn to a method of identifying a susceptibility locus for a disorder that is characterized by reduced mitochondrial function, glucose intolerance, or insulin intolerance in a subject.

Group 5, claim(s) 47, 48, drawn to a method of determining if a subject is at risk of developing a disorder which is characterized by reduced mitochondrial function.

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Group 6, claim(s) 78, drawn to a method of detecting statistically-significant differences in the expression level of at least one biomarker belonging to a biomarker set, between the members of a first and second experimental group.

Group 7, claim(s) 93, drawn to a method of identifying an agent that regulates expression of OXPHOS-CR genes.

The inventions listed as Groups 1-7 do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: Unity of invention between different categories of inventions will only be found to exist if the specific combinations are present. These combinations include:

- 1) a product and special process of manufacture of said product,
- 2) a product and a process of use of said product,
- 3) a product, a special process of manufacture of said product, and a process of use of said product,
- 4) a process and an apparatus specially designed to carry out said process,
- 5) a product, a special process of manufacture of said product, and an apparatus specially designed to carry out said process.

The allowed combinations do not include multiple products, multiple methods of using said product, and methods of making multiple products as claimed in the instant application, see MPEP § 1850.

In addition to this, Polansky, WO 01/60408 A2, teaches that heregulin increases GABPalpha expression specifically (Schaffer, 1998) (Polansky, page 32, parag. under "Heregulin"). It is noted that while Polansky do not specifically indicate that one of the

biological responses, as listed in claim 1 occur, it is implied that the biological responses would be affected with the increase in GABPalpha expression.

Each of the groups is distinct from the other as each method is used to arrive at different results/products.

The claims are further restricted.

Groups 1-3 are drawn to the use of an agent. According to the specification, page 22, an agent may be a polypeptide, a nucleic acid, or a chemical compound (specification, page 22, 2<sup>nd</sup> parag.), and one agent must be elected. Each of the agents is distinct from each other because each comprises a different structure and different biological activity. The search and examination for each agent is burdensome because the searches are not coextensive.

Group 1, claim 6, is drawn to modulating the expression level or transcriptional activity of Err-alpha or Gabp and either expression level or transcriptional activity must be elected. In addition to this, claim 6 is drawn to affecting Err-alpha, Gabp, or both proteins, with an agent, and either Err-alpha, Gabp, or both proteins must be elected. "Expression level" and "transcriptional activity" are distinct from each other because these are two distinct biological processes. One affects the production of mRNA; the other affects activity of protein. As for the election of Err-alpha, Gabp, or both proteins, the proteins are distinct from each other because each has a particular biological activity. The search and examination for Err-alpha, Gabp, both proteins and whether the nucleic acid levels or protein activity are affected by the modulator is burdensome because the searches are not coextensive. Note that upon election of the protein(s)

and “expression level” or “transcriptional activity,” the claims will be read on the elected elements.

Group 1 encompasses methods that are in vivo (see claim 11) and in vitro and one must be elected. In vivo methods are distinct from in vitro methods because they require different method steps. A search and examination for in vivo and in vitro methods are burdensome because the searches are not coextensive.

Group 2 (see claim 17) is drawn to determining if an agent increases a property of Err-alpha or Gapb and one must be elected. The properties are a) expression of Err-alpha or Gapb, b) activity of Err-alpha or Gapb, or c) the formation of a complex with PGC-1. The properties are distinct from each other because each requires different and distinct biological events to occur. In addition to this restriction, the proteins, Err-alpha and Gapb, are restricted from each other as each has a different biological activity. As such, an election of Err-alpha or Gapb is required. The search and examination for each property and for both proteins are burdensome because the searches are not coextensive.

Group 3 (see claim 35) is drawn to reducing the metabolic rate in a subject comprising administering an agent which decreases the expression or activity of i) Err-alpha, ii) Gabpa, iii) a gene having a Err-alpha binding site, a Gabpa binding site, or both, or iv) a transcriptional activator which binds to an Err-alpha binding site or to a Gabpa binding site and one activity of the agent on one particular product must be elected. First, with regard to activity, expression or activity, one must be elected. mRNA expression is distinct from activity of a protein as these are different biological

processes. The search and examination of expression and activity are burdensome because the searches are not coextensive. Second, with regard to the election of a particular product, Err-alpha, Gabpa, a gene that has a Err-alpha or Gabpa binding site or both binding sites, and a transcriptional activator are all distinct from each other and one must be elected. Each of these products is distinct from each other because each has a different biological activity. The search and examination for each product is burdensome because the searches are not coextensive.

This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

Group 1, claim 1 lists 9 distinct biological responses, a) to i), and one must be elected. The responses are distinct from each other because to determine each of the biological activities requires different method steps. A search and examination of each biological response is burdensome because the searches are not coextensive.

Should Applicant elect "in vivo" in Group 1 (see restriction, above), a further election of species of the disease (see claim 15) in which the claimed method is carried out must be elected. Each of the diseases is distinct from each other because each has a unique etiology and pathology. The search and examination of each disease is burdensome because the searches are not coextensive.

Group 3 is drawn to reducing the metabolic rate in a variety of patients and one disease or disorder from claims 36-38 must be elected. Each of the diseases or

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disorders is distinct from the other as each has its own pathology. It is noted that "cancer" (claim 36) is distinct from "cancer cachexia" (claim 38) as cancer is interpreted to concern issues such as tumors, cell proliferation, and metastases, while cachexia is interpreted to concern issues of tissue wasting. The search and examination for each disease are burdensome because the searches are not coextensive.

Group 4 is drawn to a method of identifying a susceptibility locus for a disorder and one gene selected from Tables 10-12 must be elected. Each of the genes listed in Tables 10-12 are distinct from each other as each gene has a different biological activity. The search and examination of each gene are burdensome because the searches are not coextensive.

Group 4 is drawn to identifying a susceptibility locus for a disorder and one disorder must be elected (see claims 45 and 46). Each of the diseases or disorders is distinct from the other as each has its own pathology. The search and examination for each disease or disorder are burdensome because the searches are not coextensive.

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. The reply must also identify the claims readable on the elected species, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims



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are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

The following claim(s) are generic:

Claims 1-7, 11-16 of Invention 1 are generic for the biological responses, as listed in claim 1.

Claims 1-7, 11-16 of Invention 1 are generic for the disorders that affect humans.

Claims 35-38 of Invention 3 are generic for the disorders.

Claims 42-46 of Invention 4 are generic for the genes that comprise a polymorphism and may be implicated in a disorder.

Claim 42-46 of Invention 4 are generic for disorders in which a susceptibility locus is identified.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the

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record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Joanne Hama  
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